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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,833	05/03/2005	Masahiro Kajino	Q101061	7356
23373	7590	11/24/2008	EXAMINER	
SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. SUITE 800 WASHINGTON, DC 20037			MABRY, JOHN	
ART UNIT	PAPER NUMBER			
	1625			
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11/24/2008	PAPER			

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/533,833	<b>Applicant(s)</b> KAJINO ET AL.
	<b>Examiner</b> John Mabry, PhD	<b>Art Unit</b> 1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 18 August 2008.

2a) This action is FINAL.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 11-23,26,28 and 29 is/are pending in the application.

4a) Of the above claim(s) 18 and 19 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 11-17,20-23,26,28 and 29 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 0/18/08

4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_

5) Notice of Informal Patent Application

6) Other: \_\_\_\_\_

***Response to Amendment(s)***

Applicant is respectfully reminded that it is required that all claims be amended to elected group. Examiner also warns Applicant not to introduce new matter when amending.

Applicant's response on August 18, 2008 filed in response to the Office Action dated April 4, 2008 has been received and duly noted.

In view of this response, the status of the rejections/objections of record is as follows:

***Status of the Claims***

Claims 11-17, 20-23, 26, 28 and 29 are pending and rejected.

Claims 1-10, 24-25 and 27 have been cancelled.

Claims 18-19 are directed towards non-elected subject matter.

Claim 29 is new.

***Foreign Priority***

Foreign priority is acknowledged in view of certified priority document being received May 3, 2005.

***Specification Objections***

Objection to title has been overcome in view of Applicant's amending the title.

***Claim Objection***

Claim objection to the term "a nitrogen-containingnitrogen-containing ring." has been overcome in view of Applicant cancelling claim.

***35 USC § 112 Rejection(s)***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The 112-2<sup>nd</sup> rejection of claims 11-17, 20-23, 26, 28 and 29 regarding the term "substituted" have been overcome in view of Applicants cancelling and amending the claims.

The 112-2<sup>nd</sup> rejection of claims 11-17, 20-23, 26, 28 and 29 regarding the preamble "...a pharmaceutical composition" have been overcome in view of Applicants amending the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The 112-1<sup>st</sup> rejection of claims 11-17, 20-23, 26, 28 and 29 regarding the terms "prodrug" have been overcome in view of Applicant's amendment.

The 112-1<sup>st</sup> rejection of claims 11-17, 20-23, 26, 28 and 29 regarding the scope of enablement for "optionally substituted" have been not overcome in view of Applicants amending the claims (see scope of enablement rejection in previous Office Action).

Variable R3, in particular, has not overcome rejection even in view of Applicant's amendment. Applicant has amended R3 as follows:

R<sup>3</sup> represents an optionally substituted phenyl group, an optionally substituted aromatic heterocyclic group or an optionally substituted cycloalkyl group (i) a C<sub>3-5</sub> cycloalkyl group, (ii) a phenyl group or (iii) a 5- to 10-membered aromatic heterocyclic group containing one or two kinds of 1 to 4 hetero atoms selected from a nitrogen atom, a sulfur atom and an oxygen atom in addition to carbon atoms, which may be substituted with a substituent selected from the group consisting of a halogen atom, cyano, C<sub>1-6</sub> alkyl optionally substituted with a halogen atom, C<sub>1-6</sub> alkoxy optionally substituted with a halogen atom, C<sub>1-6</sub> alkyl-carbonylamino, a 5- or 6-membered aromatic heterocyclic group and C<sub>1-6</sub> alkylthio.

Applicant is not enabled for the scope of the claimed invention as described in previous Office Action (see scope of enablement rejection) in view of Applicant's amending the claims. Variable R3 of most current set of claims corresponds to variable A as described in Restriction Requirement of elected Group I (without traverse) which was examined – "...-Z-A where -Z- is unsubstituted methylene (-CH<sub>2</sub>-) or substituted with unsubstituted alkyl and -A is phenyl substituted with H, alkyl, halogen, alkoxy,

haloalkylalkoxy, -S alkyl, -NHalkyl,..." The amended definition of R3 clearly falls outside of the scope of elected group. Only the scope of the elected group was examined.

R3 being "optionally substituted" was rejected as described in previous Office Action. Applicant's response to scope of enablement rejections is as follows:

At page 7 of the Office Action, claims 1-8, 11-17, 20-26 and 28 are rejected under 35 U.S.C. § 112, first paragraph, as not enabled with respect to the claimed constituents being "optionally substituted."

Applicants herewith amend the claims without prejudice or disclaimer. Applicants' amendments overcome the rejections.

Withdrawal of the § 112 rejections is requested.  
Applicant has not fully responded to Examiner's rejection.

#### ***Claim Rejections - 35 USC § 102***

Claims 11-17, 20-23, 26, 28 and 29 rejections are withdrawn under 35 U.S.C. 102(b) as being anticipated by Lin et al (US 4,871,749 and US 4,791,120). The claims are newly rejected under 35 U.S.C. 103(a) below due to Applicant's amendments. The Applicant argues that this compound is excluded from instant claims. Examiner acknowledges Applicant's exclusion; however, according to Applicant's claims, the claimed compounds are deemed obvious. The instant application claims compounds and compositions of Formula I"" wherein R2b=ethyl, R1b= 4-ethyl-2-thiazolyl, Z1=CH2 and R3=phenyl.

Claims 11-17, 20-23, 26, 28 and 29 rejections are withdrawn under 35

U.S.C. 102(b) as being anticipated by Kudzma et al (J. Med. Chem. 1989, 32, 2534-42).

Due to Applicant's amendments, said claims are considered obvious under 35

U.S.C. 103(a) as described below.

***Claim Rejections - 35 USC § 103***

The rejection of claims 11-17, 20-23, 26, 28 and 29 under 35 U.S.C. 103(a) as being unpatentable over Lin et al (US 4,831,192 A) is maintained for reasons of record in the previous office action.

Applicant argues that the benzyl group is used as a protective group in Kudzma et al. However, Examiner did not reject said claims over Kudzma et al; Examiner rejected said claims over Lin et al. Lin et al does not teach this subgenus as a protective group.

Applicant also argues that Examiner failed to state a reason that would have prompted a person of ordinary skill in the art to obtain Applicant's claimed compounds from the compounds of Lin et al. Examiner respectfully disagrees. Lin et al states that compounds of Formula I''' allow rapid regain of muscle coordination, respiratory depression, heart rate decrease and arterial pressure decrease (see column 1, lines 31-39). The instant applicant states that compounds of Formula I''' are involved in smooth muscle constricting action, blood pressure rising action, treatment of muscular skeletal disease and cardiac vascular disease (see pages 3-4 of Specification). The compounds of Lin et al and instant application are drawn to treat similar and overlapping diseases,

disorders and conditions.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

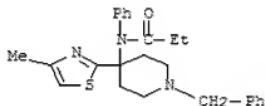
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 11-17, 20-23, 26, 28 and 29 rejections are rejected under 35 U.S.C. 103(a) as being unpatentable over Lin et al (US 4,871,749 and US 4,791,120) and Kudzma et al (J. Med. Chem. 1989, 32, 2534-42).

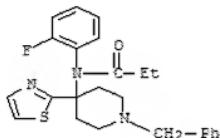
The instant application claims compounds and compositions of Formula I''' wherein R2b=ethyl, R1b= 4-ethyl-2-thiazolyl, Z1=CH2 and R3=phenyl.

**Scope & Content of Prior Art MPEP 2141.01**

Lin et al discloses compounds and compositions of Formula I<sup>\*\*\*</sup> wherein R2b=ethyl, R1b= 4-methyl-2-thiazolyl, Z1=CH2 and R3=phenyl (see Example 3, column 10). Pharmaceutical compositions are taught in column 3, lines 42-42. The oxalate salts are taught in column 3, lines 50-51.



Kudzma et al discloses compounds and compositions of Formula I<sup>\*\*\*</sup> wherein R2b=ethyl, R1b= 4-methyl-2-thiazolyl, Z1=CH2 and R3=2-fluoro-phenyl (see compound 8e, page 2535, Scheme 1) (PTO-1449).



**Differences between Prior Art & the Claims MPEP 2141.02**

The instant claims differ from Lin at the alkyl substituent on the R1b thiazole: Applicant's 4-ethyl versus Lin's 4-methyl, which are considered obvious (H versus CH<sub>3</sub> in the case of Kudama). Applicant's -CH<sub>2</sub>CH<sub>3</sub> versus Lin's -CH<sub>3</sub>. An ethyl and methyl are deemed obvious variants (*In re Wood*, 199 USPQ 137).

***Prima Facie Obviousness, Rational & Motivation MPEP 2142-2413***

It would be obvious for one of ordinary skill in the art to simply alter the chain length of an alkyl in order to achieve the instant claimed invention as described above. Also, Lin teaching that the thiazole (R1b) can be substituted with lower alkoxy, lower alkoxy lower alkyl, lower alkyl or a combination thereof (see column 2, lines 21-25). Thus, said claims are deemed obvious.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Conclusion***

Applicant is respectfully reminded that it is required that all claims be amended to elected group. Examiner also warns Applicant not to introduce new matter when amending.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John Mabry, PhD whose telephone number is (571) 270-1967. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's primary examiner can be reached at (571) 272-0684, first, or the Examiner's supervisor, Janet Andres, PhD, can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/John Mabry/  
Examiner  
Art Unit 1625

/Rita J. Desai/  
Primary Examiner, Art Unit 1625